The Seven Deadly Syndromes

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A few terms to better understand this discussion:

- Subjective: A complaint. Often unverifiable ("I don't feel well", Headache, pain)
- Objective: Measurable. Temperature, blood pressure, MRI, Lab results
- Syndrome: A collection of subjective complaints often seen together
- Diagnosis: Determination of the nature of the cause of a disease. A concise technical description of the cause, nature, or manifestations of a condition, situation, or problem. This should be based upon OBJECTIVELY DEFINED LAB/RADIOLOGIC/PATHOLOGIC FACTORS, NOT ASSUMPTION ("I know it when I see it")

TERMS:

- Differential Diagnosis: the determination of which one of several diseases may be producing the pathology and symptoms. This is MANDATORY in medicine, as there may be multiple causes simultaneously present
- Polypharmacy: The use of multiple medications
- Narcotic: A drug or substance affecting mood or behavior. May be illegal
- Benzodiazepines: Valium, Lorazepam, clonazepam
- Antidepressants: SSRI, SNRI, tricyclics
- Anti-convulsants: Gabapentin, Lyrica
- Muscle relaxers: Flexeril, baclofen, Soma
- Drug-drug interactions: A potential reaction between two prescribed drugs. may be fatal under certain circumstances

Disease state: Pathological process MEDICINE SHOULD BE SCIENTIFIC

- **Pathology** is the study of the causes and effects of disease or injury.
- Pathology can be demonstrated by objective testing (lab studies, MRI, x-rays, EKG, tissue samples under the microscope). NOT Assumption
- Clinical progress and outcomes of most disease processes can be tracked through appropriate, objective monitoring (ex: Pneumonia monitored with CXR, Heart problems with EKG, Echo, etc.)
- The diagnosis of these 7 “Syndromes” should follow the standard diagnostic guidelines.
- This is especially true if patients do not improve with treatments.

The Seven Deadly Syndromes

- Neuropathic Pain Syndrome
- Fibromyalgia Syndrome
- Complex Regional Pain Syndrome
- Chronic Pain Syndrome
- Post Lumbar Laminectomy Syndrome
- Post concussion Syndrome
- Carpal Tunnel Syndrome

A Closer look at these Syndromes:

- It is inappropriate to assign diagnoses for patients without the differential diagnostic process.
- These syndromes have standard treatment guidelines to follow
- Our own evaluation of the Ohio BWC data (on CRPS) indicate only 1 patient had 6 basic diagnostic testing performed.
- Treatment often has no meaningful, long term effectiveness.
- We are not saying or implying there is nothing wrong with these patients or that their symptoms are not real. We are concerned that the workup was incomplete, the conclusions faulty and interventions ineffective. This can be failure to diagnose.
- Our obligation to any patient is to make the correct diagnosis and to provide safe, effective care.
- If the symptoms continue, "do NOT leave any stone unturned".

Neuropathic Pain Syndrome:

- Caused by damage or disease to a peripheral nerve
- May be associated with altered sensation or pain in the distribution of that nerve. Symptoms may be episodic or continuous.
- MAY BE OBJECTIVELY VALIDATED by EMG, lab studies (high blood sugar, low vit B12, evidence of alcoholism, etc.)examination findings to include anatomic distribution of complaints, measurements for atrophy, skin changes, anatomic weakness and consideration of alternative explanation (Differential Diagnosis).
- Underlying causes may be associated with diabetes, thyroid, multiple sclerosis, stroke, Herpes zoster, HIV, nutritional deficiencies, toxins, malignancies, immune disorders, trauma, congenital, etc.
- Treatment should be directed to underlying cause
- There is no "arm nerve"….there are 8 of them. Symptoms should be anatomically identifiable (Clinical Medicine)

Fibromyalgia Syndrome:

- Characterized by widespread muscle pain, fatigue, altered sensations, GI complaints, HA, mood swings, anxiety, sleep problems, depression. Seen more often in middle aged/post menopausal women.
- There are no known diagnostic tests for this condition.
- Therefore, a "diagnosis of exclusion"
- There is no known cause, although Vitamin D deficiency has been associated.
- Note the presentation is based upon largely unprovable subjective complaints.
- Causal suspicion with viral infections, genetics, physical/emotional trauma, stress, autoimmune diseases
- Treatment directed to symptoms of pain, antidepressants, anti-convulsants

Complex Regional Pain Syndrome (CRPS)

- A default condition
- Sometimes associated with extremity "trauma" but diagnostic criteria refer to "inciting event", not trauma
- Interventions with poor outcomes (treating the wrong diagnosis)
- Over 100 names for this condition, almost as many diagnostic criteria (Borchers, Autoimmunity Rev 2014)
- "INVENTED DIAGNOSIS" (Chang, Autoimmunity Rev 2018)
- Extensive differential diagnosis which is rarely investigated (next slide).
- Treatments of unproven efficacy (Sympathetic blocks, Ketamine, etc.)
- Almost never seen outside of compensation setting

CRPS I DIFFERENTIAL DIAGNOSIS(PAINFUL LIMB)

Hereditary nerve disorders

Toxic: (alcohol. lead, insecticides, solvents)

Chemotherapeutics: (cancer drugs, antibiotics, steroids)

Trauma: (cellulitis, entrapment neuropathy)

Systemic: (Lupus, RA, peripheral vascular disease, renal/liver failure, cancer and paraneoplastic syndromes, sarcoidosis)

Infectious: (Hepatitis B and C, HIV, leprosy, lyme disease, herpes simplex/cytomegalovirus, syphilis)

Endocrine: (Diabetes, hypothyroidism, impaired glucose tolerance)

GI: (Crohn's disease, ulcerative colitis, celiac disease)

Chronic Pain Syndrome

- Definition: Pain complaints exceeding 90 days
- Definition of Pain: "An unpleasant subjective experience" (IASP)
- Diagnosis based solely on subjective complaints.
- Multiple "interventions" may result in increased symptoms (opiate hyperalgesia) and actually may prolong recovery or increase symptoms
- These include drug-drug interactions, complications of injection "therapy", addiction, and death.

Lumbar Post-Laminectomy Syndrome

- This term should be directed only to those who have residual low back pain after a Lumbar Laminectomy
- Term is often applied to anyone with low back pain after any lumbar surgical procedure
- There are no diagnostic criteria otherwise
- Treatment is directed to symptoms only and usually includes polypharmacy with opiates, muscle relaxers, NSAIDS, Anti-depressants, sleeping medications, anti-convulsants, pain pumps, and spinal cord stimulator without explanation.
- Often over-medicalization of procedures and medications with very little improvement in outcomes.

Post Concussion(al) Syndrome or Mild Traumatic Brain Injury

- Term applied to collection of subjective complaints arising after head trauma
  - loss of consciousness of approximately 30 min or less; after 30 min an initial Glasgow Coma Scale (GCS) of 13–15; and posttraumatic amnesia (PTA) not greater than 24 h
- Like all diagnoses in medicine, diagnostic criteria **must have been met.**
- Complaints usually unprovable, such as Headache, dizziness, "fogginess", unclear thinking, nausea, balance problems, amnesia, difficulty concentrating, fatigue, memory problems, insomnia
- Diagnostic testing is often normal, except for psychometrics (MMPI, Millon)
- Differential diagnosis includes PTSD, Affective disorders, Stroke, cardiac arrhythmia, malingering, factitious disorder
- Workup may include psychometric testing, as well as thorough neurologic exam. MRI, etc.

Carpal Tunnel Syndrome (CTS)

- Altered function of median nerve at the wrist
- Symptoms characterized by numbness, weakness tingling Thumb, index, middle fingers palmar side of hand.
- Causes include age, female gender, post-menopausal status, diabetes, thyroid problems, obesity, repetitive awkward forceful hand activity with vibrating tools/equipment.
- Differential diagnosis rarely performed. A relationship with work commonly presumed regardless of assignment or activity
- If underlying cause is not addressed, surgery unlikely to be of benefit
- Usually, symptoms clear in 4-6 weeks after uncomplicated surgery
- Make sure EMG performed by medically trained physician with electrodiagnostic certification and training

Syndromic treatments

- Differential diagnosis rare
- Treatment is directed to subjective complaints and therefore often unsuccessful
- Pain gets treated with pain medications, anticonvulsants, antidepressants, anxiolytic medications.
- Reports of "spasms" are unreliable unless determined by electrodiagnostics. RX with muscle relaxers, benzodiazepines
- Not uncommon to have multiple medications ("polypharmacy") to address gradually increasing symptoms. Increasing symptoms should pose a "red flag" for unrelated causes.
- Response to treatment usually poor, prolonged and followed by requests for more diagnostics, more medications, more injections, etc.
- Drug-drug interactions and side effects may explain increasing symptoms

Drug-drug interactions (DDI)

- Every drug can react to your body system
- But simultaneous use of multiple drugs can produce an interaction between these medication. This is called DDI
- These can be mild, moderate or MAJOR
- Always referred to as "potential" reactions as we are all internally different, so individual responses can vary
- "Major potential DDI" is contraindicated as it can be fatal
- We uncover Major potential DDI among our evaluations weekly
- This may be an explanation for treatment failures and deaths

Ohio Workers Compensation Data: 2000-2018, de-identified data

- Over a million claims
- Identified each of the 7DS and assessed for total number, PTD, RTW status, Deaths, Narcotic use and daily dose, combination polypharmacy. We excluded anyone hospitalized within 30 days of injury
- Drug categories include:
- Narcotics -(all opiate, opioids)
- MR- Muscle relaxers
- Anti-depressants- amitriptyline, Zoloft, Celexa, etc.
- Anxiolytics- Valium, Lorazepam, xanax
- Anticonvulsants (Gabapentin, Lyrica)

7DS: SOME FACTS FOR CONSIDERATION

- Diagnostic tests for the 7DS are very limited.
- That means the diagnosis cannot be "proven"
- Historic information is crucial, but often overlooked or ignored
- There are no objective clinical findings for most of these conditions
- **There is an extensive differential diagnosis** regarding these conditions, almost never investigated
- It Is rare for a differential diagnostic process to be performed.
- The assessment of the 7DS is usually based on "I know it when I see it'
- Given these facts WHAT ARE WE REALLY TREATING?

7DS: Studied Outcomes

- How many subjects received each diagnosis?
- How many were treated only with narcotics?
- How many were treated with narcotics and muscle relaxers and antidepressants and Benzodiazepines?
- How many were permanently disabled or never returned to work?
- How many are dead?
- Keep in mind, these conditions have unproven pathology, lack diagnostic capability and are supposed to reflect a "default" status

Studied outcomes: NEUROPATHIC PAIN

- Neuropathic pain total 1109 claims
- PTD + no RTW=36+297=333 never RTW (30%)
- 34 dead
- 174 taking only narcotics (5 dead)
- **16%- 178 taking Narcotics + Benzo+ MR+ AD +AC (5 dead)**

FIBROMYALGIA

- Total diagnosed 764
- PTD + no RTW=26+161=187 (25%)
- Total dead=26
- Narcotics only 107 (14%)
- 132 taking Narcotics+Be+nzo+ MR+ AD + AC (17%)

CRPS

- CRPS total 1090 claims
- PTD + no RTW=90+494=584 never RTW (54%)
- **40 dead**
- 135 taking only narcotics (1 dead)
- **273 taking Narcotics+Benzo+ MR+ AD +AC (2 dead) (25%)**

CRPS

- CBC, CMP, GGT, EMG, UDS, ESR, Psych (one patient)
- NONE had a basic differential diagnostic profile done
- POOR OUTCOMES DUE TO INCOMPLETE WORKUP and Failure to diagnose

Chronic Pain Syndrome

- Chronic pain syndrome total 109 claims
- PTD + no RTW=15+59=74 never RTW (68%)
- 5 dead
- 8 taking only narcotics (1 dead)
- 46 taking Narcotics+Benzo+ MR+ AD +AC (42%) (2 dead)

Lumbar Post Laminectomy Syndrome (LPLS)

- LPLS total 919 claims
- PTD + no RTW=175+ 467= 642 never RTW (70%)
- 34 dead
- 15 taking only narcotics (0 dead)
- 494 taking Narcotics+Benzo+ MR+ AD +AC (54%) (24 dead)

Post Concussion(al) Syndrome (PCS)

- PCS total 1103 claims
- PTD + no RTW=39+346=385 never RTW (35%)
- 16 dead
- 141 taking only narcotics (1 dead)
- 110 taking Narcotics+Benzo+ MR+ AD +AC (10%) (4 dead)

Carpal Tunnel Syndrome (CTS)

- CTS total 6493 claims
- PTD + no RTW=125+1181=1306 never RTW (20%)
- 228 dead
- **3251taking only narcotics (114 dead)**
- 321 taking Narcotics+Benzo+ MR+ AD +AC (5%) (18 dead)

STANDARDIZED MORTALITY RATIOS Randolph, D. et al.

- This is determined through a ratio of Observed deaths/Expected Deaths
- Ohio general population is the comparison group (CDC data)
- Male and Female combined

Group	OBS Deaths	EXP	SMR	p value	95%CI
NSAIDs only	45	82.69	0.54	<0.001	(0.4,0.72)
Sch2 only	***545***	***622.52***	***0.88***	***0.002***	***(0.8,0.95)***
Sch2+ASH	51	36.25	1.41	0.014	(1.06,1.84)
Sch2+MR/AD	296	278.47	1.06	0.29	(0.95,1.19)
Sch2+ ASH+MR/AD	251	144.12	1.74	<0.001	(1.54,1.97)

SMR Schedule II, MED 50-100MED (Male and Female combined)

Group	OBS Deaths	EXP	SMR	p value	95%CI
NSAIDs only	45	82.69	0.54	<0.001	(0.4,0.72)
Sch2 only	142	173	0.82	0.017	(0.69,0.96)
Sch2+ASH	17	13.41	1.27	0.33	(0.76,1.99)
Sch2+MR/AD	260	155.96	1.67	<0.001	(1.47,1.88)
Sch2+ ASH+MR/AD	115	51.8	2.22	<0.001	(1.84,2.65)

SMR >100mg MED (male and female)

Group	OBS Deaths	EXP	SMR	p value	95%CI
NSAIDs only	45	82.69	0.54	<0.001	(0.4,0.72)
Sch2 only	108	104.55	1.03	0.74	(0.85. 1.24)
Sch2+ASH	13	5.91	2.2	0.0035	(1.22,3.67)
Sch2+MR/AD	300	287.27	1.04	0.45	(0.93, 1.17)
Sch2+ ASH	52	25.1	2.07	<0.001	(1.56,2.7)
MR/AD					

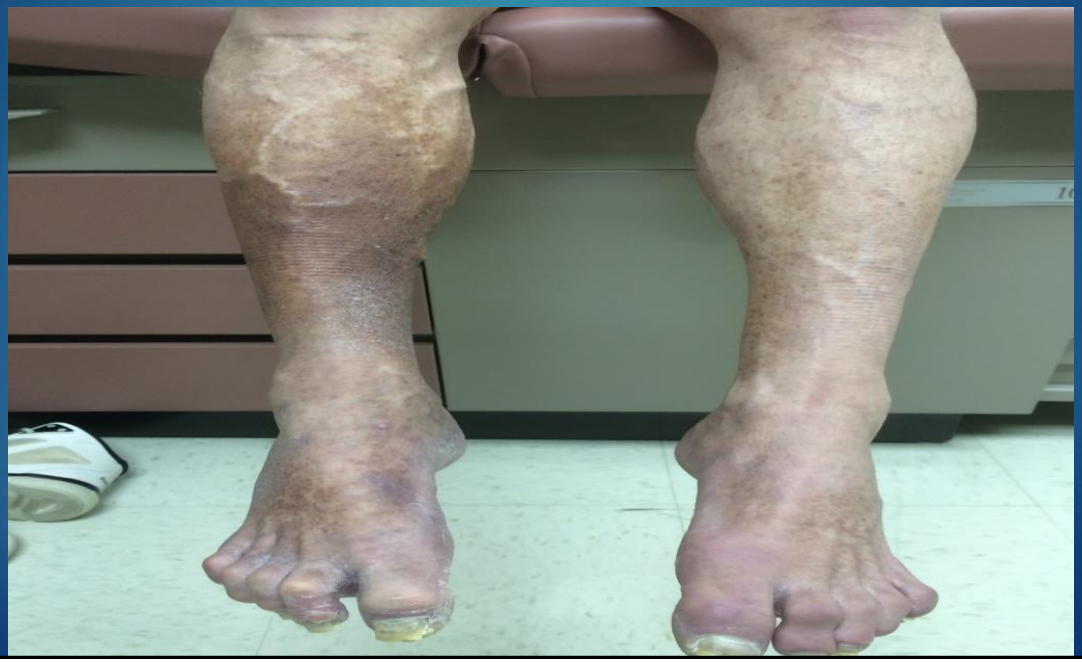
CASE FOR CONSIDERATION

- 42 yo WM, Date of injury 2002, injured right ankle descending from a ladder. Off work since. Diagnosed with "RSD" or "CRPS I". Developed DVT with PE, vague GI complaints, BS elevation 200, "adrenal insufficiency, sleep apnea, hypogonadism, decreased testosterone, HTN, symptoms "spread" to all 4 extremities. He has lost all his teeth. He uses a motorized WC and crutches.
- Treatment involved multiple injections including sympathetic blocks, facet blocks, ESI, RFA all without benefit despite multiple repeats. Attempts at SCS unsuccessful.
- Meds include over 700 MED with Exalgos, Actiq suckers (1600mcg 6x/day), Clonidine, 3 different testosterone preparations, multiple anti depressants including atypical antipsychotics

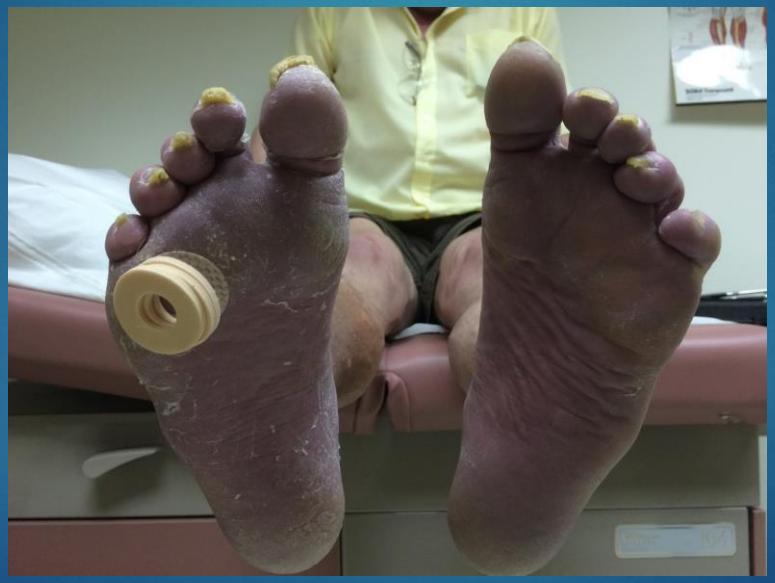
CRPS 1 ?????

- Review of polypharmacy include 12 major (potentially lethal) DDI
- Despite all interventions, he reports increasing symptoms
- During course of exam lasting over 2 hours, he used 2 Actiq suckers
- SSDI granted in 2003
- Extensive lab/procedural requests were discussed. He discussed these with his attorney and refused. He continues to see his POR, travelling 2 hours for office visits and refills monthly.
- Diagnostic possibilities include RA, Lupus, Buergers disease, addiction, somatoform disorder, anxiety, depressive disorder

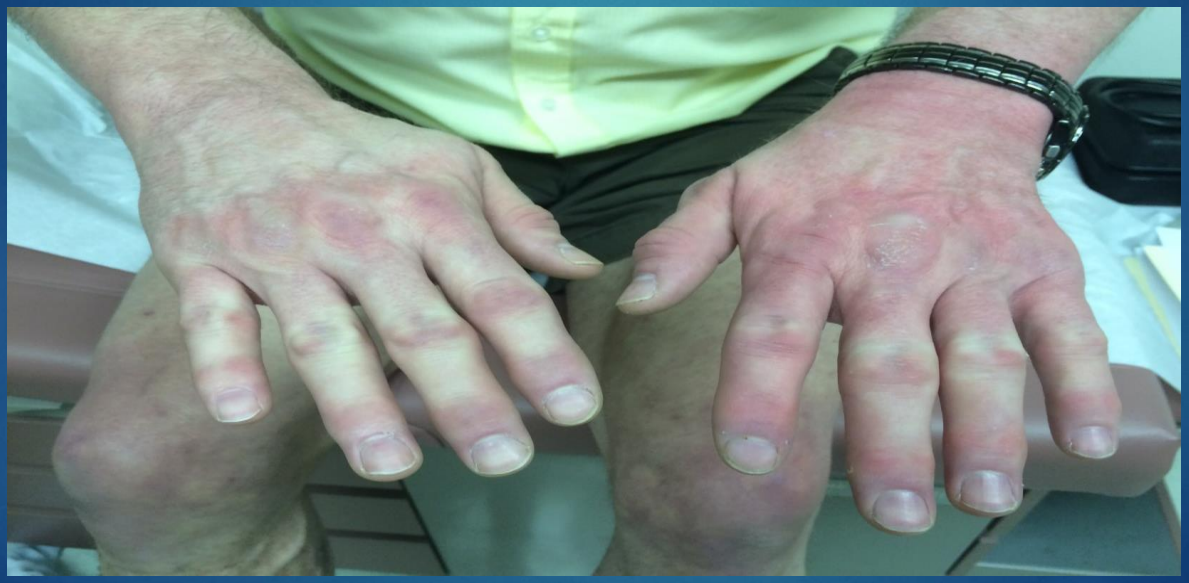
Sprained ankle and CRPS I



CRPS



CRPS?



CRPS I is a "Default condition" ONLY!!!

- No pathologic explanation
- No confirmatory lab studies
- No "true positives"
- No scientific explanation
- No attempt at a differential diagnosis
- Medicine by Hubris
- Safety/health risks due to failure to diagnose,
- Treatment clearly unsafe and ineffective.
- PARADIGM LOST!!

WHAT IS THE DIAGNOSIS/PROGNOSIS?

- NOT CRPS !!!...no evidence of a differential diagnosis anywhere.
- Painful extremities with evidence of vascular compromise and dysautonomia (Subject for another discussion)
- Autoimmune condition heads the list
- Evidence of addiction/substance use disorder
- Urgent need to detox and discontinue harmful drug combinations
- Early demise of patient is predictable. Rules of the system provide very few options but enforced continuation of harmful medications and combinations is lunacy.
- INSANITY IS DEFINED AS REPEATING THE SAME ACTION AND EXPECTING A DIFFERENT RESULT.

Serotonin Syndrome: A toxic response to drug combinations

More accurately named "Serotonin Toxicity", as this is the true pathologic process

Symptoms include :

confusion, hallucination, seizure, extreme changes in blood pressure, increased heart rate, **fever**, **excessive sweating**, shivering or shaking, blurred vision, muscle spasm or stiffness, tremor, incoordination, stomach cramp, **nausea**, **vomiting**, and **diarrhea**.

Severe cases may result in coma and even death. (Drugs.com)

"Serotonin Syndrome"

Common Drug combinations which can result in Serotonin Syndrome:

SSRI Antidepressants (Celexa, Zoloft, Paxil)

SNRI Antidepressants (Trazodone, Cymbalta, Effexor)

Bupropion

Tricyclics (amitriptylene, Pamelor)

Antimigraine (Imitrex, Tegretol)

Lithium

Opiates, opioids (from tramadol to Fentanyl)

Illicits (cocaine, amphetamines)

Over-the counter cough, cold preparations and herbal supplements

- (St. John's wort, Ginseng, Nutmeg, dextromethorphan
- THIS IS NOT A COMPLETE LIST

Frequency of Serotonin Syndrome diagnosis in Ohio BWC database

- Not found
- This is not because it does not exist
- This is because it is not recognized and/or not considered in the evaluation of the treated population
- The common usage of the involved referenced drugs in combination speaks to the likely prevalence of this as a problem
- Incidence of SS 14.3% among those who overdosed on SSRI (Ibister GK, et al. Relative Toxicity of Selective Serotonin Reuptake Inhibitors (SSRIs) in Overdose. J Toxicol Clin Toxicol. 2004;42(3):277-85.
- Incidence in those taking combination meds is unknown

TAKE HOME POINTS:

- Beware the "syndrome"
- Healing is a normal process
- Prolonged unresponsiveness to standard care should raise a red flag
- A second opinion should be provided by a clinically trained physician (Internal Medicine is a good place to start)
- Raise a red flag if the differential diagnosis is nowhere to be found
- Red Flag for "I know it when I see it"
- If the clinical picture does not make sense to you, call for help. You are most likely right.
- Death is not considered a good outcome, and can be avoided by sound medical practices of a CLINICIAN